Monday Morning Practice Pearls #30

Why does the FDA inspect IRBs and what do they review?

The FDA's Bioresearch Monitoring (BIMO) Program is a comprehensive program of on-site inspections and data audits intended to monitor all aspects of the conduct and reporting of FDA-regulated research. The BIMO Program involves inspection of the following:

- Clinical Investigators (CI)
- Sponsor/Monitor/Contract Research Organization (CRO)
- Bioequivalence/Good Laboratory Practice
- IRB
- Radioactive Drug Research Committee (RDRC)

The FDA inspects the IRB to determine if the IRB is operating in compliance with current FDA regulations (i.e., 21 CFR Parts 11, 50, 56, 312 and 812) and the IRB's Standard Operating Procedures (SOPs). There are 2 categories of IRB inspections:

- Routine/Surveillance inspections which are conducted every 5 years, or
- Directed/For-Cause inspections which generally result from a complaint, CI misconduct, or safety issues for a trial or site.

What studies will the FDA review?

The studies selected for review are preferably ones that were initially approved within the previous 3 years and are currently ongoing at the time of the inspection. The FDA may also select one study that has been through a continuing review cycle. Generally, the studies are selected using the following prioritization:

- Studies identified for a directed inspection, if any
- Studies using novel regulatory mechanisms (e.g., exploratory IND studies) or involving cutting edge technologies (e.g., cell, gene, and tissue-based therapies)
- Studies involving vulnerable populations (e.g., pediatric studies, consent exempt studies)
- Device studies that involve the IRB's determination as to whether a device study is significant risk (SR) or non-significant Risk (NSR);
- Other safety and efficacy studies conducted under and IND or IDE
- Studies where privacy/confidentiality protections may be of particular concern (e.g., HIV studies)
- Studies for which no FDA research permit is required (e.g., certain marketed drugs and non-significant risk devices)
- Comparison studies of one or more marketed products with an investigational product

What happens during the inspection?

During the inspection, the FDA will interview appropriate people (i.e., IRB Chair, IRB Administrator) and will typically review and make copies of the following:

- IRB Membership Rosters
- IRB Written Procedures
- IRB Meeting Minutes
- Documents related to FDA studies reviewed including:

- Protocol and Investigator Brochure
- Consent form
- Correspondence between the IRB and the clinical investigator
- Correspondence between the IRB, FDA, and appropriate institutional officials that report any unanticipated problems involving risk to human subjects or others and any instances of serious or continuing noncompliance with the regulations

How does the FDA classify the outcome of an inspection?

The outcome of the FDA inspection will be one of the following:

- No Action Indicated (NAI) - No objectionable conditions or practices were found during the inspection, or the significance of the documented objectionable conditions found does not justify further FDA action.
- Voluntary Action Indicated (VAI) - Objectionable conditions were found and documented, but the reviewing Center (e.g., CDER, CBER) is not prepared to take or recommend any further regulatory action because the objectionable conditions do not meet the threshold for regulatory action
- Official Action Indicated (OAI) - An OAI recommendation is appropriate when regulatory violation(s) uncovered is/are significant/serious and/or numerous, and the scope, severity, or pattern of violations(s) support a finding that:
  - Subjects participating in studies approved by the IRB would be or have been exposed to an unreasonable and significant risk of illness or injury; or
  - Subjects' rights would be or have been seriously compromised; or
  - Data integrity or reliability is or has been compromised.

What are some of the common deficiencies found during an IRB inspection?

The most common IRB deficiencies include:

- Inadequate initial and/or continuing review
- Inadequate SOPs
- Inadequate membership rosters
- Inadequate meeting minutes
- Quorum issues
- Inadequate communication with Investigator and Institution

Resources:

- Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors FDA Institutional Review Board Inspections Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors: FDA Institutional Review Board Inspections http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126555.pdf
- FDA Compliance Program Guidance Manual (CPGM) for Institutional Review Boards http://www.fda.gov/downloads/ICECI/EnforcementActions/BioresearchMonitoring/UCM133768.pdf